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## Original Research Article

# Monoclonal antibodies for cancerous conditions in essential medicine list: An experience from a tertiary hospital in Bengaluru, India

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## ABSTRACT

**Background:** Globally, cancer is emerging as a major public health problem. Monoclonal antibodies are extensively used for cancerous conditions at tertiary hospitals. Many of these are not easily available for patients seeking treatment from public sector. It is difficult for poor patients to afford these drugs on individual basis.

**Aims:** The aim of our study is to calculate the prescribed daily dose of monoclonal antibody in cancerous conditions, to know the number of monoclonal antibody present in the essential drug list and to know the average total number of drugs prescribed in generic names.

**Materials and Methods:** The average dose of the monoclonal antibody used is calculated and the common conditions for which it is used is tabulated and the drug usage is noted for both genders. The number monoclonal antibody present in the list of essential medicine of India and WHO is compared. The average total number of drugs prescribed in generic names is calculated.

**Results:** Average prescribed dose calculated was 382 mg for Trastuzumab, 455mg for rituximab. Only a few monoclonal antibodies were found in who essential drug. Only Trastuzumab and rituximab monoclonal antibody were found in the essential drug list of India. While, Trastuzumab is the most commonly (61%) prescribed drug in the generic form.

**Conclusion:** The study concludes that Trastuzumab is the commonly used monoclonal antibody followed by Rituximab and Bevacizumab. Only Trastuzumab and rituximab were found in Indian essential drug list. Measures for Inclusion of other monoclonal anti bodies can be made by the policy decisions.

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## 1. Introduction

Globally, the disease management has taken a stage of paramount importance and the health care management system has emerged to be a challenge. Among the disease management the treatable disease assumes the highest importance. The least available avenues for the health systems to measure the diseases of least occurrences would be to look into the drug utilization of these lifesaving drugs at the tertiary hospitals. It also becomes important for the hospital authorities (both public and private) to monitor the

utilization of these drugs to include them in their essential list of medicines for making it accessible for the needy patients.

Cancer is the second leading cause of death and is responsible for 10 million deaths per year.<sup>1</sup> Approximately 70% of deaths occur in low- and middle-income countries. The commonest problem that prevails across the countries is late-stage diagnosis and lack of access to diagnosis and treatment. Comprehensive treatment is known to be available in 90% of high-income countries and 15% in low- and middle-income countries.

The incidence of cancer is seen to be increasing in India and it has become an area of prime importance for health

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care management. The breast cancer is considered to be the commonest cancer among females.<sup>2</sup> There has been lot of advancement among cancer treatment and autoimmune diseases monoclonal antibodies assumes importance as they target specific receptors like VEGF and HER2.<sup>3</sup> Monoclonal antibodies intend to target tumor antigens and drugs like rituximab are target specific.

The drugs like monoclonal antibodies used for cancer quite often do not have optimal daily dose requirement as it has varied usage across the patients and depends on the treating oncologist, severity and type of the disease. Though, there has some efforts by American therapeutic committee to provide defined daily doses for all the drugs not much has been said on monoclonal antibodies. The drug utilization studies help the manufacturers to design appropriate dosage strength and their formulations for the betterment of the affected population.<sup>4</sup> The health policy makers are relying on drug utilization studies to make drug available, affordable and accessible for those who are in need.<sup>5</sup> Hence, our study aims to calculate the prescribed daily dose of monoclonal antibody in cancerous conditions, to know the number of monoclonal antibody present in the essential drug list and to know the average total number of drugs prescribed in generic names

## 2. Materials and Methods

### 2.1. Study design

A cross-sectional study using the routine hospital data from the medical records department at hospital.

### 2.2. Settings

The ESIC Medical College and PGIMSR, a tertiary care hospital which is centrally located at Bengaluru, Karnataka, India. It is a teaching hospital with 750 bed capacity with more than 1000 outpatient per day. The hospital provides its services only to insured persons under the ESIC scheme for workers working at industries. The hospital caters to patients from all over the state of Karnataka. The hospital has a separate specialized oncology department and has empaneled other cancer hospital centers in the city for diagnosis and treatment.

### 2.3. Study population and period

All the patients attending the department of oncology during February 2019 to June 2019 were included in the study.

### 2.4. Statistics

The data was collected from medical records department for the study period. The data was entered in a data collection tool for the variables like age, gender, usage of drug, indication of drug, diagnosis for the frequently used monoclonal antibodies. The prescribed daily dose is

calculated using the formula: total dose given / number of days.<sup>6,7</sup> The defined daily dose for the drugs are noted by the website [https://www.whocc.no/atc\\_ddd\\_index](https://www.whocc.no/atc_ddd_index).<sup>8</sup> The drugs were looked for their presence in essential drug lists of WHO and India. The data from data collection format was entered into the Microsoft excel. The data was cleaned to remove duplicates and missing values and was analysed using EpiData Analysis software (version 2.2.2.182, EpiData Association, Odense, Denmark). The frequencies and proportions were calculated for all the variables and cross tabulation was made for select variables.

### 2.5. Ethics consideration

The administrative permission and approval were obtained for usage of data from the hospital authorities. The Ethics approval for the conduct of the study was obtained from Ethics Review Committee of ESIC Medical College and PGIMSR, Bengaluru.

## 3. Results

During the study period, a total of 181 patients were included. Of which 145(80%) were females and 36(20%) were males. The characteristics of the study population is shown in Table 1. More than 57 (31%) patients belonged to the age group of 51-60 years. Among females, the following conditions has highest number of patients: carcinoma breast (74%), MBC (9%) and carcinoma cervix (4%). Among males, the following conditions has highest number of patients: carcinoma lung (28%), CLL (12%), giant cell tumour and multiple myeloma (8%). The commonest drugs used were: Trastuzumab (60%), Rituximab (9%) and Bevacizumab (5%). The calculated daily defined dose, Prescribed Daily Dose for various drugs and the availability of drugs in essential drug lists of WHO and India are shown in Table 2. Most of the drugs in our study did not have defined daily dose from the American therapeutic committee. The average given dose for Trastuzumab is 382 mg, Rituximab is 455 mg and Cetuximab is 300 mg. Only two drugs (Rituximab, Trastuzumab) were listed in both the essential medical list of WHO and India. Only 7/12 drugs were in WHO list and 2/12 drugs were listed from India. Among the monoclonal antibodies prescribed in the generic form, Trastuzumab was found to be in 67/110 prescriptions treated with trastuzumab containing preparation.

## 4. Discussion

It is one of the first study conducted in the region to understand the utilization pattern of monoclonal antibodies. The study findings reveal that monoclonal antibodies are commonly used to treat cancerous conditions and majority of the drugs are not listed in essential medicine list of India.

As described in the previous literatures, monoclonal antibodies are prescribed for patients with many cancerous

**Table 1:** Characteristics of study population diagnosis and drug utilization stratified by gender (N=181)

	Characteristics	Female	Male	
		(n=145)	(n=36)	
		n (%)	n (%)	
Age (yrs)	< 40	20 (71)	8 (29)	
	41-50	38 (86)	6 (14)	
	51-60	48 (84)	9 (16)	
	61-70	35 (85)	6 (15)	
	> 70	04 (36)	7 (64)	
Diagnosis	B Cell CLL	0 (0.0)	2 (8.0)	
	B Cell Lymphoma	1 (0.8)	0 (0.0)	
	C NSL	1 (0.8)	0 (0.0)	
	Ca Breast	99 (74.4)	0 (0.0)	
	Ca Cervix	6 (4.5)	0 (0.0)	
	Ca FOM Ent ENT	2 (1.5)	0 (0.0)	
	Ca GEJ	1 (0.8)	1 (4.0)	
	Ca Lung	0 (0.0)	7 (28.0)	
	Ca Ovary	4 (3.0)	0 (0.0)	
	Ca Prostate	1 (0.8)	0 (0.0)	
	Ca Recto Simoid	1 (0.8)	0 (0.0)	
	CLL	1 (0.8)	3(12.0)	
	Follicular Lymphoma	0 (0.0)	1 (4.0)	
	Gaint Cell Tumour	0 (0.0)	2 (8.0)	
	Hodgkins Lymphoma	1 (0.8)	0 (0.0)	
	MBC	13 (9.8)	0 (0.0)	
	MBL	1 (0.8)	0 (0.0)	
	MM	0 (0.0)	1 (4.0)	
	Multiple Myeloma	0 (0.0)	2 (8.0)	
	NHL	0 (0.0)	1 (4.0)	
	NSCLC	0 (0.0)	1 (4.0)	
	Post Cardiac Transplant	0 (0.0)	1 (4.0)	
	Lymphocyte PTC			
	Primary Gastric Lymphoma On	1 (0.8)	0 (0.0)	
	ART			
	PTCD	0 (0.0)	1 (4.0)	
	SLL	0 (0.0)	2 (8.0)	
	Drugs	Adalimumab	1 (25.0)	3 (75.0)
		Bevacizumab	10 (100)	0 (0.0)
		Cetuximab	2 (100)	0 (0.0)
		Cetuximab + Irinotecan	1 (100)	0 (0.0)
		Denozumab	1 (12.5)	7 (87.5)
Golimimumab		1 (33.3)	2 (66.7)	
Infliximab		1 (50.0)	1 (50.0)	
Nivolumab		1 (16.7)	5 (83.3)	
Nivolumab + Pacitaxel		0 (0.0)	1 (100.0)	
Omalizumab		1(50.0)	1 (50.0)	
Ramicurimab+Pacitaxel		1(100)	0 (0.0)	
Ramucirumab		0(0.0)	1 (100.0)	
Rituximab		7(43.8)	9 (56.3)	
Rituximab+Bendamustine		1(20.0)	4 (80.0)	
Rituximab+Oxaliplatin		1(100)	0 (0.0)	
Secukinimab		3(60.0)	2 (40.0)	
Trastuzumab		110(100)	0 (0.0)	
Trastuzumab+Docetaxel		2(100)	0 (0.0)	
Trastuzumab+Zolendionate+Pacitaxel		1(25.0)	0 (0.0)	

**Table 2:** The calculated DDD, PDD and availability of drugs in essential drug lists

Name of the drugs	DDD	PDD	WHO (2019)	EDL India (2015)
Adalimumab	2.90	40	Yes	No
Bevacizumab	NA	394	Yes	No
Cetuximab	NA	300	No	No
Denozumab	NA	120	No	No
Golimumab	1.66	50	Yes	No
Infliximab	3.75	NA	Yes	No
Nivolumab	NA	240	Yes	No
Omalizumab	16.0	150	No	No
Ramucirumab	NA	NA	No	No
Rituximab	NA	455	Yes	Yes
Secukinimab	10.0	150	No	No
Trastuzumab	NA	382	Yes	Yes

conditions either as a single drug or in combinations with other drugs.<sup>9</sup> Though, there are no specified DDD and PDD for many of the drugs used in these situations.<sup>8</sup>

The study findings have following programmatic implications. First, many drugs do not have DDD and PDD to guide the clinicians for management of patients. It is necessary to conduct further studies nationwide to determine the dosages for various conditions and provide consensual statements or guidelines for the clinicians to follow religiously. Second, many drugs are not listed in Indian medical list though listed in WHO list. The issue is of great concern since many hospitals in India especially under public sector procure the drugs based on the essential medical list of the ministry of health and family welfare. Any absence in the list essentially affects the patients and the families affected by these clinical conditions. Monoclonal antibodies are in pipeline for many similar conditions.<sup>10</sup>

The study has few limitations. The exact DDD for monoclonal antibodies were not available through ATC classification because of inter-individual variations and because of large variations in the dosages. The DDD obtained by our study should be generalized cautiously as the figures were drawn from a single treating hospital. Studies have been done to calculate the PDD for anticoagulant in India.<sup>11</sup> Some of the monoclonal antibodies are found to be useful for Corona virus in experimental studies.<sup>10</sup> There are many studies for antimicrobial agent consumption with regard to their prescribed daily dose<sup>12,13</sup> but very few for the anticancer Monoclonal antibodies further research is recommended involving larger sample size and centers.

## 5. Conclusion

The utilization of monoclonal antibodies is common for many cancerous conditions. The monoclonal antibodies listed in the essential drug list is sub-optimal. Further

research is recommended to arrive at DDD and PDD for monoclonal antibodies in the country.

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## 7. Conflict of Interest

None.

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